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CHARACTERIZATION OF TAP AMBR250 DISPOSABLE BIOREACTORS, AS A RELIABLE SCALE-DOWN MODEL FOR BIOLOGICS PROCESS DEVELOPMENT

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In recent years, biologic drugs such as antibodies, biosimilars and fusion proteins have continued to enter into the pharmaceutical pipeline. To shorten cell culture process development and accelerate clinical trials and regulatory filing, the disposable Advanced Microscale Bioreactors (Ambr 250) has burgeoned to be a useful tool due to the advantages of highly automated control and short turnaround. However, the traditional early stage upstream process development is normally conducted in 3L or 5L bioreactors. The usage of Ambr 250 instead of 5L bioreactors in the development has many benefits, but also brings necessity to establish a scale-down model of Ambr 250 to mimic 5L bioreactors. In our study, a comprehensive kLa characterization of Ambr 250 was conducted to define optimal operational conditions. Three different scale-down approaches, i.e. dimensionless volumetric flow rate (vvm), Power per unit volume (P/V) and kLa models have been evaluated using different cell lines. Since Design of Experiments (DoE) is often used in upstream process development, the response of Ambr 250 bioreactors to process parameters such as temperature, pH, seeding density, feeding strategy were compared to those of 5L bioreactors. In addition to process development, the suitability of Ambr 250 in the clone selection, which is traditionally conducted in 5L bioreactors, was investigated using six different clones. These studies showed that Ambr 250 generates similar profiles of cell growth and protein production to 5L and 1000L bioreactors. The data suggest that Ambr 250 can be used for early stage clone selection and process development as the replacement for traditional glass 5L bioreactors, and it has great potential applications in late stage process validation and process characterization.